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Survival advantage in Asian American end-stage renal disease patients[1]

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Survival advantage in Asian American end-stage renal disease patients.

Background. An earlier study documented a lower mortality risk for end-stage renal disease (ESRD) patients in Japan compared with the United States. We compared the mortality of Caucasian (white) and Asian American dialysis patients in the United States to evaluate whether Asian ancestry was associated with lower mortality in the United States.

Methods. The study sample from the U.S. Renal Data System census of ESRD patients treated in the United States included 84,192 white or Asian patients starting dialysis during May 1995 to April 1997, of whom 18,435 died by April 30, 1997. Patient characteristics were described by race. Relative mortality risks (RRs) for Asian Americans relative to whites were analyzed by Cox proportional hazards regression models adjusting for characteristics and comorbidities. Population death rates were derived from vital statistics for the United States and Japan by age and sex.

Results. Adjusting for demographics, diabetes, comorbidities, and nutritional factors, the RR for Asian Americans was 0.75 ($P = 0.0001$). Race-specific background population death rates accounted for over half of the race-related mortality difference. For whites, mortality decreased as the body mass index (BMI) increased. For Asians, the relationship between BMI and survival was u-shaped. The ratio of Asian American/white dialysis death rates and the ratio of Asian American/white general population death rates both varied by age in a similar pattern. The population death rates of Asian American and Japanese were also similar.

Conclusion. Among dialysis patients, Asian Americans had a markedly lower adjusted RR than whites. The effect of BMI on survival differed by race. Compared with the respective general population, dialysis patients had the same relative increase in death rates for both races. The difference in death rates between the United States and Japan does not appear to be primarily treatment related, but rather is related to background death rates.

[1] **See Editorial by Breyer-Lewis, p. 2528.**

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End-stage renal disease (ESRD) in Asian Americans is an important topic for many different reasons. Although Asian Americans make up only 3.7% of the United States' population, they are by far the fastest growing racial group [1]. Between the years 1980 and 1990, the Asian population in America doubled [2]. Furthermore, ESRD incidence rates per million population are higher for Asians than for Caucasian Americans (whites), although they are not as high as for African Americans (blacks) and Native Americans (354 cases per million Asians vs. 199 cases per million whites) [3].

Previous studies comparing the survival of ESRD patients in the United States and Japan found that Japanese patients had higher survival rates compared with U.S. patients [4]. In a comparison of five-year renal replacement therapy (RRT) survival rates of the United States and Japan from 1982 to 1987, Held et al reported the age- and diabetes-adjusted mortality relative risk (RR) for the Japanese patients to be 25% lower than for U.S. patients (RR = 0.75). The age-adjusted RR for nondiabetic Japanese was 0.71, and for diabetic Japanese, it was 0.81. The results of this and a subsequent study have stimulated American nephrologists to evaluate their standards and practices [5].

The demographics and characteristics of the RRT populations in the two countries differed; the Japanese were younger and less likely to be diabetic. However, the better outcomes were confirmed in each adult age group for both diabetic and nondiabetic patients. There were also other difficulties in comparing the U.S. and Japanese RRT patients in that the rate of kidney transplantation is much lower in Japan than in the United States [3]. However, the comparison of all ESRD patients should have favored the United States because of the benefits of transplantation [4].

A major obstacle in comparing patients in the two countries is that the racial composition, traditions, and cultures of U.S. patients are different from those of the Japanese patients (99.9% of DNA is common, and values

are almost identical; however, there are differences). The U.S. Renal Data System (USRDS) has reported that different racial groups have different mortality risks for ESRD, and whites have the worst mortality [3]. Japan is almost entirely comprised of people of Japanese or of other Asian descent. In the United States, the U.S. Census Bureau statistics for 1996 includes whites (82.8% of total U.S. population), blacks (12.7%), Native Americans (0.9%), and Asians and Pacific Islanders (3.7%) [1]. Although the U.S. Asian population is a mixture of different ethnic groups, a comparison of the mortality risk between white and Asian ESRD patients within the United States may help to explain the difference between ESRD mortality rates in the United States and Japan. If the difference in ESRD mortality for the United States versus Japanese were similar to that for U.S. white versus U.S. Asian, the difference may be greatly accounted for by the dissimilarities in the background populations and not in the dialysis technique. If the U.S. Asians have survival that is more similar to the U.S. whites than to the Japanese, then the difference with Japan more likely would be a response to differences in dialysis practice and technique, and not to patient population differences.

This study examines a national census of adult dialysis patients who were incident between May 1995 and April 1997, to examine the differences in patient population characteristics and survival in U.S. whites and U.S. Asians in an attempt to compare the adjusted survival for these two groups.

METHODS

Data sources

All data for this study came from the USRDS Standard Analysis Files [6]. This study was comprised of patients who had a Medical Evidence Form signed by a physician between May 1, 1995, and April 30, 1997, with a first dialysis service date on or after January 31, 1995. Excluded from this study were patients who were younger than the age of 18, or those who died or were transplanted in the first 90 days of ESRD. Patients were followed until transplantation, loss to follow-up, or to the end of the study on December 31, 1997.

Race data came from two sources, the social security files, which contain self-reported race (primary source), and the Medical Evidence Form, which is filled out by the dialysis center. Patients with a missing cause of ESRD were excluded from the analyses. Only patients who were classified as "white" or "Asian" were used in these analyses, unless otherwise specified. To allow comparisons of Asians with all other patients, the racial groups "Native American," "black," and "white" were combined as "non-Asian."

Ranges of acceptable values for different patient characteristics such as height, weight, and serum albumin are shown in Table 1. For comorbid conditions, the response of "yes" was counted as having the condition, and answers of "no," "unknown," or "cannot disclose" were considered as not having the condition. Hemoglobin and hematocrit had more detailed methods for cleaning, which considered the consistency of both values and clinical plausibility. The values for blood urea nitrogen (BUN), serum creatinine, and glomerular filtration rate (GFR) [7, 8] were obtained before the patient began dialysis.

The body mass index (BMI) was computed as the weight divided by the height squared in kg per meter squared, and the patients were divided into five-unit BMI groups (BMI group). The percentage of diabetic ESRD was then calculated for each BMI group by race.

The calculation of average dialysis dose (Kt/V) by race group and the methods for survival analyses adjusting for Kt/V are the same as used in waves 1, 3, and 4 of the USRDS Dialysis Morbidity and Mortality Study (DMMS). The methodology for this more detailed study of over 17,000 hemodialysis patients is described in the USRDS 1998 Annual Data Report [3].

Statistical analysis

The *t*-test was used to compare the mean values for scaled variables, including age, weight, and hemoglobin for whites and Asians. The chi-square test was used to compare the Asian American versus white gender and comorbidity distribution.

Cox proportional hazards regression models were used to determine the mortality risk ratios of Asian patients relative to white patients. These models were adjusted for different characteristics such as race, sex, diabetes as primary cause of ESRD, nutrition, laboratory values, and comorbidities. The exact adjustments are detailed in Table 3. To determine if the RR for race varied by sex or diabetes, interaction variables were included in the Cox model. Based on these results, the Asian:white mortality risk ratios were calculated separately for those with diabetes as the primary cause of ESRD and for those with all other causes of ESRD. Each race was divided into race-specific BMI quintiles, and the Asian:white risk ratios were also assessed by BMI quintile. Other models determining Asian:white risk ratios were calculated by primary cause of ESRD and then by geographic region. Another set of models that examined the RR of each race-specific BMI quintile compared with the middle BMI quintile for whites was created.

For the "Asian versus all others" comparison, the mortality risk ratios were calculated by the Cox proportional hazards model, and the Asian risk ratio was calculated relative to that of whites, blacks, and Native Americans combined.

The death rates of the dialysis patients were calculated

Table 1. Summary of patient characteristics by race

Patient characteristics	*Acceptable range*	Mean or percent		*P* value
		White	Asian	
Male	%	55.9	50.4	0.001
Age at incidence	>18 years	63.1	61.2	0.0001
Height	122–214 cm	168.1	161.2	0.0001
Weight	37.5–125 kg	71.9	61.6	0.0001
BMI	kg/m^2	25.5	23.6	0.0001
Serum albumin	0.8–6.0 g/dl	3.3	3.2	0.0001
Hematocrit	9–60%	28.6	27.8	0.0001
Hemoglobin	3–18 g/dl	9.6	9.3	0.0001
BUN	24–250 mg/dl	94.8	97.0	0.0001
Serum creatinine	3–33 mg/dl	8.1	9.1	0.0001
GFR Levey formula	ml/min	7.1	6.2	0.0001
GFR Walser formula	ml/min	5.6	3.6	0.0001
Primary cause of ESRD[a]	% yes			
Diabetes		44.0	46.5	0.001
Hypertension		23.6	22.1	0.025
Glomerulonephritis		11.6	16.4	0.001
Cystic kidney disease		3.3	1.9	0.001
Other urologic cause		2.5	1.5	0.001
Other cause		11.2	7.0	0.001
Unknown cause		4.0	4.7	0.015
Number of comorbidities		1.9	1.3	0.0001
Comorbidities	% yes			
AIDS		0.1	0.0	0.038
Cancer		5.7	2.1	0.001
Cardiac arrest		1.1	0.5	0.001
Cardiac dysrhythmia		6.7	3.6	0.001
Cerebrovascular accident		9.1	6.6	0.001
Congestive heart failure		35.1	25.8	0.001
COPD		8.5	2.8	0.001
Diabetes mellitus		50.9	51.2	0.674
HIV positive		0.1	0.0	0.064
Hypertension		69.8	68.0	0.011
Ischemic heart disease		27.4	15.9	0.001
Myocardial infarction		10.8	5.2	0.001
Peripheral vascular disease		17.0	7.2	0.001
Smoker		6.3	1.9	0.001

[a] Overall P value = 0.0001

by determining the number of deaths that occurred during the study and the number of total patient days alive. The ratio of deaths per patient day was converted to deaths per patient year to compare with the death rates of the general population. SAS 6.12 was used for all descriptive and survival analyses.

RESULTS

Patient characteristics

There were 125,962 patients in the original USRDS data set whose start of ESRD was recorded during the two-year period. Excluding patients under 18 years of age and other races, there were 79,721 whites (94.7%) and 4471 Asians (5.3%). The demographics for the two race groups differed. In general, the whites were older, taller, heavier, and had laboratory values that were considered to be more predictive of survival, as shown in Table 1.

The Asians had a lower average count of comorbid conditions (1.28) compared with whites (1.93, P = 0.0001). This racial difference held true for patients with diabetic ESRD and for those who had ESRD from different causes, with diabetics having more comorbidities than nondiabetics. White diabetics had the highest average number of comorbid conditions (white diabetes mellitus average = 2.69, white non-diabetes mellitus average = 1.33, P = 0.0001). Asian diabetics had fewer comorbidities than white diabetics but more than Asian nondiabetics (Asian diabetes mellitus average = 2.06, Asian non-diabetes mellitus average = 0.60, P = 0.0001). Asians had a lower percentage of every comorbid condition except for diabetes (Table 1). Additionally, Asians had 5% more diabetes than whites at every BMI value, and both races had an increase of percentage of diabetes with increasing BMI.

The distribution of primary causes of ESRD differed overall between the races (P = 0.001). Asians had more

Table 2. Asian patient demographics by region and mortality risk ratio (RR) compared to whites (RR = 1.0) in Cox model adjusting for age, sex, diabetes by region

Region (U.S. States)	Percent Asian in region	Percent of total Asians	RR	*P* value
1 (AL WA OR CA HI)	19.1	60.0	0.66	0.0001
2 (KY TN MS AL)	1.1	1.1	1.00	0.9987
3 (MT ID WY NV AK UT CO AZ NM)	2.7	2.7	0.73	0.2136
4 (TX OK AR LA)	1.6	3.3	0.76	0.2011
5 (NH ME VT MA RI CT)	1.9	1.9	0.80	0.4440
6 (WV VA MD DC VA NC SC GA FL)	4.2	13.4	0.89	0.1791
7 (MI WI IL IN OH)	1.7	5.3	0.84	0.2658
8 (ND SD NE KS MN IA MO)	1.7	2.2	0.56	0.0824
9 (NY NJ PA DE)	3.4	10.2	0.48	0.0001
10 Total U.S.	5.3	100.0	0.652	—

Table 3. Mortality risk ratios (RR) of Asians compared to whites (RR = 1.0) in Cox models by level of covariate adjustment

Covariates	RR	*P* value
Unadjusted	0.62	0.0001
Age	0.66	0.0001
Age, sex	0.66	0.0001
Age, sex, diab as primary cause of ESRD[a]	0.65	0.0001
Age, sex, diab, nutrition (albumin, creatinine)	0.70	0.0001
Age, sex, diab, nutrition, lab values[b]	0.69	0.0001
Age, sex, diab, comorbidity count	0.73	0.0001
Age, sex, diab, comorbidities[c]	0.73	0.0001
Age, sex, diab, nutrition, lab val, comorbidities	0.75	0.0001
By diabetes as primary cause of ESRD (Asian-diabetes interaction, *P* value = 0.0041)		
DM only: age, sex	0.73	0.0001
No DM only: age, sex	0.58	0.0001

[a] Asian-male interaction, *P* value = 0.9406
[b] "Lab values" include BUN, hematocrit, hemoglobin, pre-ESRD GFR
[c] "Comorbidities" includes the list of comorbid conditions shown in Table 1

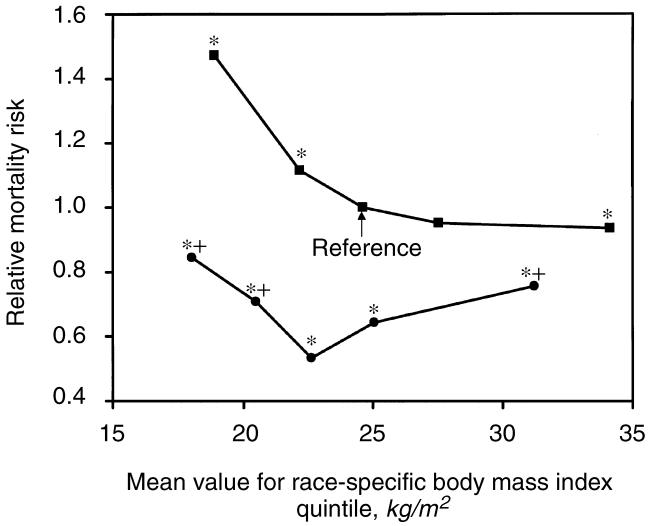

Fig. 1. Mortality risk ratios (RR) for body mass index (BMI) quintiles for whites (■) and Asians (●) on dialysis. The dialysis patients were grouped as race-specific BMI quintiles, and the RRs are shown relative to the middle BMI quintile for whites (RR = 1.0). This model also adjusted for age, sex, and diabetes as a primary cause of ESRD. $*P < 0.05$ for comparison to white middle BMI quintile; $+P < 0.05$ for comparison among Asians to Asian middle BMI quintile.

glomerulonephirits as a primary cause of ESRD (16.4 vs. 11.6% for whites) and less cystic kidney disease (1.9 vs. 3.3% for whites), but in general, the figures appeared very similar (Table 1).

The distribution of Asians starting ESRD therapy in each of the nine census regions is shown in Table 2. The majority of the Asian patients (83.6%) lived within three regions: 1 (the Pacific West Coast, Hawaii, and Alaska), 6 (the Southeast Atlantic Coast), and 9 (New York, New Jersey, Pennsylvania, and Delaware), which corresponded to the distributions of Asians in the general population.

Comparison of mortality risk

General. The unadjusted Asian:white mortality risk ratio was 0.62 ($P = 0.0001$), indicating that Asians had a 38% lower mortality rate than whites (Table 3). When adjusted for age and sex, the ratio increased to 0.66 ($P = 0.0001$) and remained relatively unchanged when adding diabetes as a primary cause of ESRD (RR = 0.65, $P = 0.0001$). There was no statistical evidence that the Asian:white RR differed by sex ($P = 0.94$), suggesting similar race effects for males and females. The model that included age, sex, and diabetes was considered the "basic" model and served as a point of reference for other models.

Nutrition. When pre-ESRD serum albumin and creatinine, indicators of nutritional state, were added to the basic model, the risk ratio rose to 0.70 ($P = 0.0001$). When other laboratory values such as hemoglobin and hematocrit were added to this model, the risk ratio basically remained the same (RR = 0.69, $P = 0.0001$). BMI was not included in either model because BMI affected survival probability very differently for the two race groups (Fig. 1).

Comorbidities. When the demographics and diabetes model were adjusted for the comorbidity count, the risk ratio was 0.73 ($P = 0.0001$), with a risk ratio 17% higher

for each additional comorbidity (RR = 1.17, $P = 0.0001$). If the model was adjusted for each of the specific comorbidities, the risk ratio was the same (0.73, $P = 0.0001$), although each condition had a different associated risk. When the nutrition and laboratory values were added to the model, the risk ratio basically remained the same (0.75, $P = 0.0001$).

Diabetes. To consider a separate effect of diabetes, each racial group was divided into two groups by the presence or absence of diabetes (DM) as a primary cause of ESRD (DM or non-DM). In the main model, Asians had a survival advantage in both the DM and the non-DM group. For DM, the Asian risk ratio was 0.73 ($P = 0.0001$), and for non-DM, it was 0.58 ($P = 0.0001$). The Asian–diabetes interaction variable was significant ($P = 0.0001$), meaning that the survival advantage that Asian DM patients had over white DM patients was smaller than expected.

Body mass index

To standardize comparison groups further, the patients in each race were divided into quintiles by BMI so that each race had five equal race-specific BMI groups. When the mortality risk for each BMI group was compared with the middle BMI quintile for whites, Asians had the biggest advantage in the lowest three BMI groups, and the highest Asian BMI group had a mortality risk not significantly different from that of the whites (Fig. 1).

For the white patients, the risk ratios of BMI quintiles relative to the middle quintile for whites showed a consistent pattern of decreasing relative mortality risk as BMI increased or stabilization above the middle quintile (Fig. 1). For the RR for Asian patients compared with the middle BMI quintile for whites, the results were dramatically different from the results for the whites, especially in the two highest BMI quintiles (Fig. 1). For Asian patients, the mortality risk was a u-shaped curve, with the lowest mortality risk at the middle BMI quintile.

Dose of dialysis

In a special analysis of the more detailed DMMS data, the Kt/V was considered for a sample of 234 Asian and 4850 white hemodialysis patients. The mean Kt/V for Asians was higher than for whites (1.30 vs. 1.23, $P < 0.01$). The mortality risk for Asians compared with whites was 0.664 without an adjustment for Kt/V and 0.675 with an adjustment for Kt/V ($P < 0.01$ for each) (abstract; Bloembergen et al, *J Am Soc Nephrol*, 9:205A, 1998).

For the main data set, no dialysis dose measures were available. However, when the basic demographics and diabetes model was adjusted for weight as an indirect correlate of dialysis dose, the Asians had a particularly large survival advantage (RR = 0.58, $P = 0.0001$). As that model was adjusted for nutritional parameters, the RR was 0.64 ($P = 0.0001$) rather than 0.70 ($P = 0.0001$), the RR for the same model without an adjustment for weight (Table 3). When comorbidities were included in the model that adjusted for weight, the RR was 0.66 ($P = 0.0001$) as compared with 0.73 ($P = 0.0001$), the RR for the same model without an adjustment for weight. When the full model, which included demographics, diabetes, nutrition, other laboratory values, and comorbid conditions along with weight, the risk ratio was even higher (0.73, $P = 0.0001$), as opposed to the risk ratio of that model without taking weight into account (RR = 0.75, $P = 0.0001$).

Table 4. Mortality risk ratios for U.S. Asians in present study versus Japanese in Held et al's study [4]

	Present study		Held study
	US Asian vs. US White	US Asian vs. all other	Japanese vs. US all races
Unadjusted RR	0.62	0.73	0.63
Adjusted RR: age, sex, diabetes	0.65	0.71	0.75

Primary cause of end-stage renal disease

The Asian to white mortality risk ratio varied slightly by primary cause of ESRD; however, it also had a significant advantage over whites among those with diabetic ESRD (RR = 0.73, $P = 0.0001$), although this benefit appeared smaller than for other causes of ESRD.

Region

It is also important to consider variations by geographic region in which the patients were dialyzed, because the mortality risk for dialysis differed from region to region. Adjusting for race, age, sex, and diabetes as primary causes of ESRD, the mortality risk of both whites and Asians for each region compared with the national risk (RR = 1.0) ranged from 0.90 to 1.11. When the whites and Asians were compared in each region, there continued to be an Asian survival advantage in most regions. Adjusting for age, sex, and diabetes, the risk ratios for Asians ranged from 0.48 to 0.89 in eight of the nine regions and was equal (RR = 1.0) in the least populated region (Table 2). The Asian-by-region interaction for each region showed no significant interaction (P values ranged from 0.13 to 0.92).

Asian versus all others comparison

For an analysis examining all four main racial groups—Native American, Asian, black, and white—patients were categorized as "Asian" or "non-Asian," with Asians comprising 3.5% of the study population. When the basic demographics and diabetes model compared Asian versus non-Asian survival, Asians had a RR of

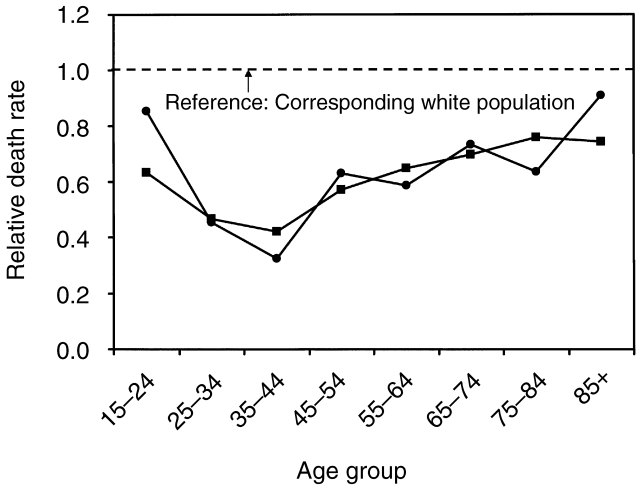

Fig. 2. Relative death rates of Asian Americans in the general population (■) and Asian Americans on dialysis (●) compared with corresponding white populations. The age-specific death rates of Asian Americans in the general population are shown relative to the death rates of whites in the general population. Also, the age-specific death rates of Asian Americans are shown relative to death rates of whites on dialysis. For example, in the 15 to 24 age group, Asian Americans in the general population had 63% of the general-population whites' death rate. Within the same age group, Asian American dialysis patients had 85% of the white dialysis patients' death rate. *The source for the general population data is in [7].

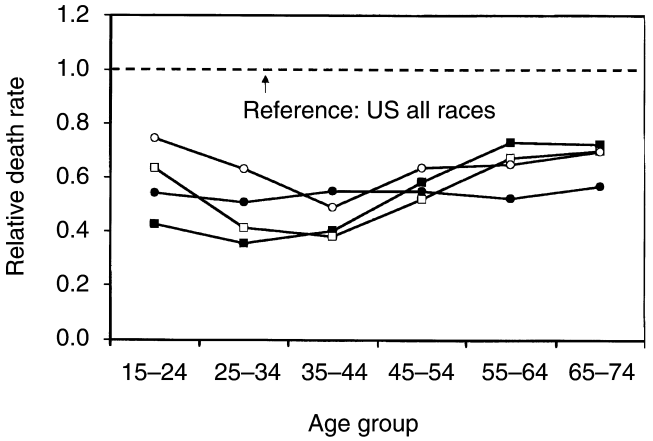

Fig. 3. Relative death rates in the general population of Japanese and U.S. Asians compared to U.S. all races. The age- and sex-specific death rates for the general populations in Japan are shown relative to the corresponding death rates of the U.S. all races. Also, the age- and sex-specific death rates of U.S. Asians in the general population were found relative to the corresponding death rates of the U.S. general population. For example, in the 15 to 24 age group, Japanese males had 43% and U.S. Asian males had 64% of the U.S. all races males' death rate. Symbols are: (■) Japanese males vs. U.S. males; (●) Japanese females vs. U.S. females; (□) U.S. Asian males vs. U.S. males; (○) U.S. Asian females vs. U.S. females.

0.71 ($P = 0.0001$) compared with the other three racial groups (Table 4). When nutrition, laboratory values, and comorbid conditions were added to this model, the Asian survival advantage lessened but remained substantial and statistically significant (RR = 0.80, $P = 0.0001$).

Background population death rates

Race (Asian vs. white) was significantly related to mortality (RR = 0.65, $P = 0.0001$ for the basic model) in the dialysis population (chi-square = 121). In a separate analysis, the age-, race-, and gender-specific background population log death rates were also significant predictors of dialysis mortality ($\chi^2 = 80$). When both race and death rates were included in the model, the RR for race was similar (RR = 0.66, $P = 0.0001$), but the chi-square statistic for race was reduced to 49. This indicated that population death rates explained more than half of the variation in mortality ($\chi^2 = 72 = 121 - 49$) that had been explained by race ($\chi^2 = 121$). Note that a chi-square of more than 4 relates to a $P < 0.05$.

Death rates in the general population

Among dialysis patients, U.S. Asian patients had a lower death rate than U.S. white patients in each of seven age groups (Fig. 2). In the entire U.S. population, U.S. Asians have a lower mortality than do U.S. whites (Fig. 2) in the same age groups, based on death rates reported by the National Center for Health Statistics [9]. The ratio of Asian to white death rates shows a similar pattern by age group for the general population as it does for the dialysis population (Fig. 2). The Japanese general population also had a lower death rate than the United States as a whole [10]. Death rates for Japan and for U.S. Asians are similar and are shown, relative to death rates for the entire U.S. population, in Figure 3.

DISCUSSION

The results of this study have shown that in the United States, Asian dialysis patients have better survival than white patients. This difference is seen when adjusting for all the factors listed in Table 1. The significantly lower mortality rate for Asian patients compared with white patients varied only slightly (RR = 0.75 to 0.62) according to the level of adjustment. Thus, Asians had at least a 25% lower mortality rate than corresponding white patients in the United States. This difference is due to factors other than those listed in Table 1.

Laboratory values

When the basic model that adjusted for age, race, sex, and diabetes also included serum albumin and creatinine, which are markers for the nutritional state, the Asian mortality risk ratio increased from 0.65 to 0.70 ($P = 0.0001$; Table 3). This implies that Asians had better nutrition than the whites. This is due to the fact that when nutrition was taken into account, the Asian survival advantage was lessened. The mean serum albumin for

the two racial groups was virtually the same (white mean albumin 3.3 mg/dl, and Asian 3.2 mg/dl), but the biggest difference was in the mean pre-ESRD serum creatinine (white mean creatinine 8.1 mg/dl, Asian 9.1 mg/dl; Table 1). The serum creatinine effect was confounded by the fact that it is both an indicator of muscle mass and also of poor renal clearance. Therefore, it is unclear from this model whether the Asians have a higher pre-ESRD creatinine because they had better nutrition or because they were started on dialysis at a later time. It is obvious, however, that the better survival for Asians is not due to starting dialysis early, that is, with better renal function.

Body mass index

When the effect of race-specific BMI quintile was examined, a higher BMI had a more protective effect for whites (Fig. 1). This confirms the findings by Leavey et al of a lower relative mortality risk with higher BMIs for U.S. dialysis patients [11]. The race-specific effect of BMI for Asian dialysis patients in this study, however, showed a different pattern with the lowest and highest BMI groups at a higher mortality risk than the middle BMI group (Fig. 1). This pattern was more consistent with the mortality trends for BMI within the U.S. general population, although the u-shaped correlation of mortality with BMI is not nearly as dramatic as that for Asian dialysis patients [12].

One may speculate that the lower mortality risk in the upper BMI groups for white dialysis patients indicates that the mortality risks associated with obesity were outweighed by the superior nutrition in these patients. For Asians, by contrast, the risk associated with obesity may outweigh the nutritional benefits

Body mass index and diabetes

The relative increase in mortality for Asian patients with higher BMIs may stem from their greater risk of diabetes associated with obesity compared with whites. The "Thrifty Gene Hypothesis" conjectures that populations that have historically undergone repeated periods of famine have developed mechanisms so that they are extremely efficient in calorie storage [2]. When these individuals are exposed to more affluent environments such as the Western diet, this adaptation becomes more of a detriment because it results in higher levels of obesity and insulin resistance. Asian American adolescents born in the United States were found to be more than twice as likely to be obese as the first-generation Asian American population [13]. Although the incidence of diabetes in Asian countries is quite low, especially in rural areas [2], studies in England showed that Asian immigrants develop diabetes at a much lower BMI than do the whites [14].

An interesting set of findings is that Asians had a nearly 25% higher incidence rate of ESRD from diabetes than whites (78.7 cases per 1 million whites/year vs. 96.9 cases per 1 million Asians/year). Also, the comorbidity count for Asians, especially for cardiovascular diseases, was much lower than for the whites. This may be explained by the fact that Asian diabetics are more likely to have renal sequelae than whites and, perhaps, not as likely to have cardiovascular consequences commonly found in whites [15, 16]. Thus, ESRD may be an earlier consequence in Asian diabetics and a later one in whites. Alternatively, Asians may be otherwise healthier than whites because their diabetes is better managed or less advanced.

Dose of dialysis

Previous studies have found that the higher the dose of dialysis that a patient receives, the better the survival [17]. It is also generally true that patients with smaller volumes or weights tend to receive higher doses of dialysis per treatment because dialysis use and length of treatment are not sufficiently individualized (abstract; Bloembergen et al, ibid). In the DMMS analyses of Asian versus Caucasian dialysis patients, we found that on average, Asian patients had a higher Kt/V than Caucasians. However, this difference would account for only 5.5% of the observed decrease in the Asian mortality rate and had virtually no effect on the mortality risk comparison in the DMMS [17]. Thus, the dose of dialysis can only explain a small fraction of the mortality differences for Asian and white dialysis patients in this study.

Region

The percentage of Asians in each region ranged widely, and they were dialyzed in regions with good, bad, and average survival when compared with the national average. In fact, two of the three largest groups of Asians were dialyzed in regions 6 and 9, both of which have a worse than the national average survival risk ratio (Table 2). Thus, it is unlikely that the Asian ESRD patient survival advantage was accounted for by the fact that they lived in regions with better than average outcomes. The range of Asian mortality risk ratios could be primarily explained by the differences in regional mortality because the Asian–region interactions were not significant.

Asian versus all others comparisons

A comparison of Asians versus the rest of the U.S. population (Native Americans, blacks, and whites) was useful for two reasons (Table 4). First, it served as a sensitivity analysis. The results for Cox proportional hazards modeling for survival of Asian versus whites were fairly consistent with results for Asian versus all others. Because the non-Asian group included blacks, who have a lower dialysis mortality rate than whites, the Asian survival advantage was somewhat smaller in this compar-

ison [3]. Second, the comparison is an excellent counterpart to the Japan versus U.S. risk ratios. The main difference is that the Japanese were compared with the entire United States, but the Asian Americans were compared with non-Asian, that is, the Native Americans, blacks, and whites. U.S. Asians, however, make up only 3.7% of the U.S. population, so their effect on overall survival was probably very minimal. Another difference was that the study compared all ESRD patients, not only dialysis patients. Because the Japanese data included very few transplant recipients, whereas the U.S. ESRD population had a higher transplant population, the Japanese survival advantage was smaller than a comparison restricted to dialysis patients would have yielded.

The age- and diabetes-adjusted mortality risk for ESRD patients in Japan versus the United States was reported as 0.75, and the risk for Asian American dialysis patients versus the rest of the U.S. dialysis patients was 0.72. Asians who were treated in the United States are of various ethnic backgrounds, making the comparison a less than perfect counterpart to the Asians in Japan. It does show by indirect comparison, however, that a similar mortality risk exists when comparing Japanese patients to Asian American ESRD patients rather than comparing Japanese to all of the United States.

Death rates in the general population

One very important consideration when comparing the survival rates of white and Asian ESRD patients is that the survival rates of the general populations of the two races differed quite dramatically, especially with the older age groups, which included the majority of ESRD patients [9]. The analyses that included race-specific background death rates showed that background population death rates explained more than half of the variation in mortality that had been explained by race. When the ratios of Asian to white death rates were compared for both the general population and for the dialysis population, they followed a similar trend across age groups (Fig. 2). This would imply that the increase in deaths from dialysis above the general population's death rate is approximately the same proportional amount for the two races at each age group. In other words, having ESRD posed the same increased risk of mortality for both races, given their background death rates. Thus, the difference in population death rates could account for the difference in dialysis survival rates between races. Therefore, we speculate that factors that contribute to the general population death rate such as genetics, diets, cultural practices, and lifestyles were then responsible for much of the disparity.

The death rates for Japan were also lower than the death rates for U.S. whites and the United States in general [9, 10]. When the death rates of the Japanese and of the U.S. Asians were compared relative to the U.S. total population, they were fairly similar, especially at the older age groups for both genders (Fig. 3). This shows that U.S. Asians represented a reasonable study substitute for the Japanese given the similar background death rates; therefore, by indirect comparison, much of the difference in risk ratios of the U.S.–Japanese studies may be accounted for by an effect that was not related to treatment. The underlying difference in the mortality rates for the general populations may greatly account for the difference in the mortality rates for the ESRD populations.

Conclusions

The mortality risk for Asian American dialysis patients is 35 to 25% lower than that for whites. Race-specific background death rates accounted for over half of the race-related mortality difference. This suggests that unmeasured factors that differed between Asians and whites deserve further study in both the general population and the ESRD population. Such factors may include lifestyle and dietary components.

Asians also have a higher risk of developing diabetes in the U.S. than they did in their native countries [2], which puts them at risk for ESRD. To prevent this, Asians may need to be monitored more carefully for diabetes, especially at younger ages and all BMI levels. Prevention and early detection of diabetes in Asians may be the most effective ways of reducing their mortality from ESRD. Also, maintaining good nutrition and avoiding obesity for Asian patients will also promote their survival. Because the effect of BMI on survival was so different for the two races, this topic should be studied further.

The results from this study suggest that survival advantages reported previously for ESRD patients treated in Japan can be explained largely, if not completely, based on differences in background death rates between the Japanese and the non-Asian U.S. populations. Previous concern that dialysis practices in the United States may be somehow inferior to those in Japan is not supported by this analysis.

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